Innovation, Industrial Development and the Regulation of Biotechnology

MARTINE KRAUS
Center for the Study of Law and Society
University of California-Berkeley
Berkeley, Calif.

We have heard many bad things about the U.S. government and government regulation; people have argued that there is either too little or too much regulation in U.S. agriculture. I am going to say a few good things about the U.S. biotechnology regulatory regime.

As you all know, regulation serves a role in safeguarding the environment and assuring food safety in the agricultural industry, and product safety, efficacy, and the consistency of the manufacturing process in the pharmaceutical industry. In both the food and pharmaceutical industries, regulation and government approval raise consumer confidence and provide companies with a powerful marketing tool — the label that says "USDA" or "FDA approved." The industry wants regulation. One only has to recall the case when Richard Godown from the Biotechnology Industry Organization and Rebecca Goldburg from the Environmental Defense Fund went jointly to the Council on Competitiveness asking the council to please not deregulate too much.

On the other hand, there is legitimate concern about regulation stifling innovation, the economic implications of regulation, and questions of international competitiveness in comparison to Europe and Japan. Over the years, the EPA has been criticized for not issuing its policy guidelines on time; the USDA for over-regulating or deregulating the wrong crops; the FDA for its long review times and requirements that were supposedly greater and more burdensome than their European counterparts.

Hence, the desire for regulation and the fear of regulation are hostages of each other. To have the seal of approval on your product, you need regulation. And regulation is always slower than no regulation.

In the case of biotechnology, the relationship between regulation and economic development has been at the center of all regulatory debates, I believe more so than in any other industry. There are three reasons for this phenomenon. First, the technology is thought to hold enormous economic promise and social benefit. Second, the industry is composed of many small start-up companies with limited resources to devote to regulatory affairs. Third, we are dealing with a sophisticated industry whose players have been, from its origin, very involved in regulatory matters. It was the scientists who came to Asilomar in the 1970s, many of whom subsequently became the founders of biotechnology start-up companies and the industry as a whole.

Many years later, the major question is: *Has regulation negatively or positively affected the development of the U.S. biotechnology industry?* I will speak to this subject in comparison to Europe. I will primarily address the regulation of plant biotechnology, but will also mention the regulation of the medical biotechnology industry because the pharmaceutical industry is prominent on this year's program. I will begin with my conclusions.

CONCLUSIONS

- *The U.S. plant biotechnology industry has been positively affected by domestic regulation and finds itself at a competitive regulatory advantage to its European counterpart.*
- *The industry has, however, been negatively affected by European regulation, in that companies hesitate to develop export crops for the European market or make investments in Europe because of perceived regulatory uncertainty.*
- *The U.S. medical biotechnology industry is domestically subject to very burdensome and stringent regulatory requirements. The industry is, however, not more disadvantaged than its European counterpart, because both regulatory regimes are costly and provide few incentives for the regulator not to err on the side of caution.*

Those conclusions, as well as the subsequent arguments, are based on studies of companies with similar operations in Europe and the United States, of which I will give you an example. I call it: A Tale of Two Companies.

A Tale of Two Companies

This is the example of a U.S. and a German based company, both of which developed a virus resistant crop, a squash, and a sugarbeet. Each crop raised very similar regulatory concerns in each country, i.e. questions of gene transfer and cross-compatibility with wild relatives. In order to gain a permit for field testing the crop, the U.S. based company faced a one-step regulatory process involving primarily the USDA-APHIS. The German based company instead faced a three-step regulatory process. The company first needed to submit its application to the national authority. The national authority in-turn sent a summary of the company's dossier to the European Commission, that, in-turn, sent the summary dossier to all member states of the European Union.

As far as the applications are concerned, the U.S. application consisted of 21 pages: seven pages on host and recipient organisms, vectors, and the genetically modified crop; four pages on the purpose of the field test, methods of data collection and harvest procedures; and one paragraph on the location and supervisory personnel. The remaining pages were graphs to support the above. The German application consisted of 100 pages: 60 pages on host and recipient organisms, vectors, and the genetically modified crop; 30 pages on the purpose of the field test and environmental risk; and 10 pages on company personnel and the supervision of the test.

Monitoring requirements in the U.S. call for only an annual field trial report, while the German company must issue a mid-trial and final environmental assessment report. In a 1995 article in *Bio/Technology*, Margaret Mellon and Jane Rissler showed that the U.S. monitoring requirements are inconsistently implemented by the USDA, while in Germany the implementation is consistent.

The initial review time for the U.S. application was 118 days. This number was reduced as the agency gained experience with the company's product and subsequent field trials were approved much more rapidly. In Germany, the approval took 175 days, followed by an appeal to court that added 32 days to the overall approval time.

The overall cost was greater in Europe than in the U.S. The estimated cost of company regulatory affairs time in the U.S. was $5,000, while in Germany it was approximately $100,000. An application fee does not exist in the U.S. but is in the range of $7,500 to $45,000 in Germany, dependent on the time and effort it takes the agency to review the application. A legal cost that is not an issue in the U.S. was estimated by the German company to be approximately $100,000.

This company comparison illustrates what I call the American regulatory advantage in plant biotechnology. The American regulatory advantage in plant biotechnology is two-fold. It consists of the regulatory regime per se, and companies' regulatory proficiency.

The Regulatory Regime

Regulatory Structure: The U.S. regulatory regime is much more centralized than its European counterpart and presents fewer regulatory hurdles to the company.

Regulatory Requirements: The U.S. regulatory requirements are far less burdensome than their European counterpart where more data regarding the environmental safety of the field test, the specifications of release conditions, and the monitoring and control of test sites are required.

Stringency: U.S. regulatory requirements are less stringent than their European counterpart.

Regulatory Style: The U.S. regulatory agencies are less legalistic than their European counterparts, clearer in their requirements, more cooperative, and less adversarial.

Review Times: Review times are consistently faster in the U.S. This is more so since the introduction of the notification process for well-characterized crops.

Regulatory Certainty: In comparison to Europe, the U.S. issued its guidelines for field-testing genetically modified crops and the commercialization of transgenic foods much earlier.

Statutory Flexibility: In the U.S., a single agency can adapt to technical progress given requirements and policies. In Europe instead such decision has to be taken by the European Commission and in part with the agreement of the European Parliament.

Other speakers may discuss whether these U.S. regulatory advantages come at a cost of increased environmental risk and reduced safety. I believe that one can have an efficient regulatory regime that safeguards the environment.

The second important part of the American regulatory advantage is the companies' regulatory proficiency or their capacity to respond to regulatory challenges.

Company Regulatory Proficiency

Company Organization: U.S. biotechnology companies are staffed with a director for regulatory affairs who is actively involved in product development. In Europe it is often the lead scientist who interacts with the regulator.

Company Experience: U.S. biotechnology companies are often experienced in dealing with environmental regulation, as often they are managed and/or staffed by former employees of the chemical industry (e.g. Mycogen's CEO formerly worked at Monsanto) or former employees of the EPA. Many European companies have never been regulated on environmental grounds. European regulators rarely move into the private sector.

Status of Regulation: Many U.S. companies consider regulation an integral part of product development. Many European companies consider regulation after they have developed their product.

Company Ingenuity: Some of the U.S. biotechnology companies established relatively early proved to be extremely innovative and imaginative in their response to regulatory challenges. European companies have not shown such ingenuity.

Following the above, it is tempting to conclude that the success of the U.S. agricultural biotechnology industry, in comparison to its European counterpart, is in major part the result of the regulatory proficiency of both the industry and government.

I conclude, however, that this is not entirely so. Regulation is only one factor in a complex innovation system. While regulation is critical at certain stages of product development, it rarely determines whether a company is founded, an entrepreneur realizes his or her plans, a product gets developed, or a technology is adopted. Hence, it does not have a direct impact on innovation per se, but is always reactive. Only in situations where there is extreme regulatory uncertainty can regulation seriously affect the development of an entire industry.

Why have the same set of techniques generated so much more industrial activity in the U.S. than in Europe (measured in terms of the number of field tests)? I suggest the difference goes beyond regulation to the industrial organization in place at the time of the introduction of the technology.

INDUSTRIAL ORGANIZATION

When biotechnology was introduced, there was an established European chemical industry (e.g. Hoechst, Bayer, BASF) that was dominated by chemists who were reluctant to enter biotechnology and had historically never been in the seed business. On the other hand, the European seed industry consisted of small- and medium-sized companies that were mostly family-owned and very traditional in nature. They were slow to innovate, reluctant to go high-tech, and had limited resources.

In contrast, the United States biotechnology industry consisted of start-up companies and established chemical companies. The start-up companies were very innovative and open to risk-taking, specialized in biotechnology techniques, and were staffed by university researchers and molecular biologists with close ties to the research community and the land grant institutions. Those companies were highly dependent on product approval because of the need to demonstrate to the venture capital community that they were worthy of funding. In most cases, the established chemical companies (Monsanto, Dow etc.) were active in crop protection and, in some cases, the seed business. In the 1970s, many U.S. chemical and petro-chemical companies had bought into seeds. The large chemical corporations also benefitted from the close proximity of innovative start-ups. Finally, the U.S. industry consisted of the world's largest seed company (Pioneer) with large resources. This U.S. industrial organization favored it over its European counterparts.

In conclusion, I wish to emphasize the following points:

- *Regulation plays an important role in assuring consumer confidence. This is particularly so in a new industry such as biotechnology.*
- *A good regulatory framework, such as the U.S. framework for the regulation of plant biotechnology, provides a support structure to industrial development but is not critical to innovation.*
- *The largest responsibility for innovation, industrial development, and the success of the regulatory process lies with individual companies, their organization, and the industry as a whole.*